REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following commentary.

I. Status of the Claims

Claim 1 and 24 have been amended with ample support in the original specification. For example, at page 28, lines 15-17; and at page 21, line 20. Claims 46-123 have been withdrawn by the Examiner, subject to a restriction requirement. Applicants reserve the right to file one or more divisional applications to pursue the subject matter of the withdrawn claims.

Because no new matter is introduced by way of this amendment, Applicants respectfully request entry of the amendment. Upon entry, claims 1-123 will be pending, with claims 46-123 withdrawn.

II. Rejection of Claims under 35 U.S.C. 112, first paragraph

Claims 35-40, 44 and 45 are rejected under 35 U.S.C. 112, first paragraph, for alleged lack of written description or enablement. Applicants respectfully traverse the rejection.

Specifically, the Examiner alleges that the specification does not teach "how the composition can result in the claimed release profile, C_{max}, T_{max} and bioequivalency." In contrast to the Examiner's assertion, the specification teaches that "by decreasing the particle size of an active agent, the surface area of the composition is increased, thereby generally resulting in an increased bioavailability" and that "[the] nanoparticulate active agents must be physically stable." See, for example, at page 1, lines 16-21; at page 4, lines 23-28; at page 5, lines 15-24; and at page 12, lines 3-10. By definition, "bioavailability" is a measurement of the rate and extent of a therapeutically active drug that reaches the systemic circulation and is available at the site of action (online Wikipedia encyclopedia). The skilled artisan would have appreciated that bioavailability is determined by a pharmacokinetic study and represented by the plasma drug concentration *vs.* time after administration. The specification further describes that bioequivalency "is preferably established by a 90% Confidence Interval (CI) of between 0.80 and 1.25 for both C_{max} and AUC" (page 18, lines 18-25). Therefore, the specification provides written support that to achieve the claimed release profile, represented by the C_{max}, T_{max}, AUC

and bioequivalency, the active ingredient must be reduced to an average particle size of less than 2000 nm and be maintained stable at this size in the presence of at least one surface stabilizer and at least one osmotically active crystal growth inhibitor, as recited in claim 1.

The specification is also enabling because it describes how to make nanoparticulate formulations (page 32 *ff*) and how the composition is stabilized in the presence of different crystal growth inhibitors (Examples 1-8).

In view of the foregoing discussion, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

III. Rejections of Claims under 35 U.S.C. 112, second paragraph

Claims 13, 24, 32-35, 37 and 39 are rejected under 35 U.S.C. 112, second paragraph, for allegedly being indefinite. Applicants respectfully traverse the rejections.

Specifically, claim 24 is rejected for containing trademarks. Claim 24 has been amended to replace the trademarks with the corresponding chemical names. Accordingly, Applicants respectfully request withdrawal of the rejection.

Claim 13 is rejected for recitation of the "liquid media," which allegedly lacks antecedent basis. Claim 1 has been amended to recite "a liquid media," thereby providing an antecedent basis for the recitation in claim 13. Therefore, the rejection should be withdrawn.

Claims 32-34, 35, 37 and 39 are rejected for recitation of "the viscosity," "the T_{max}," "the C_{max}," and "the AUC," respectively, which allegedly lack antecedent basis. Applicants respectfully disagree.

By definition, "viscosity" means "the property of a fluid that resists the force tending to cause the fluid to flow" (Random House Webster's College Dictionary, April 2001). As the skilled artisan would have appreciated, C_{max} represents the maximum concentration of a drug in the plasma, T_{max} stands for the time to reach the maximum concentration, and AUC is an abbreviation for "area under the plasma concentration time curve." Accordingly, viscosity, C_{max}, T_{max}, and AUC are properties of the composition or the active agent, hence, the base claims do not have to explicitly recite these terms to

provide antecedent basis for the dependent claims. Applicants respectfully request withdrawal of the rejections.

IV. Rejection of Claims under 35 U.S.C. §102(b)

A. Rejection Over U.S. Patent No. 5,298,262 to Na *et al.*

Claims 1-4, 6, 7, 10-15, 18 and 20-24 are rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by U.S. Patent No. 5,298,262 to Na *et al.* ("Na 1"). Applicants respectfully traverse the rejection.

Na 1 is intended to solve the problem of "aggregation of nanoparticles upon heating" (column 1, lines 26-31) by introducing into the composition a cloud point modifier, which functions to "increase the cloud point of the surface modifier" (column 1, line 66 to column 2, line 3; column 6, lines 2-11).

By contrast, the claimed invention is irrelevant to elevating the cloud point of the surface stabilizer. Rather, the claimed invention is directed to the discovery that an osmotically active crystal growth inhibitor can prevent crystal growth of the nanoparticulate active agent particles ***at ambient temperatures***. *See*, for examples, at page 21, line 20. The working examples of the present application all speak to increased stability of a composition comprising an osmotically active crystal growth inhibitor at room temperature or at 40°C.

Because Na 1's composition does not teach each and every aspect of the claimed invention, the rejection under § 102(b) should be withdrawn.

B. Rejection Over EP 0601619 to Na *et al.*

Claims 1-5, 8-15 and 17-24 are rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by EP 0601619 to Na *et al.* ("Na 2") Applicants respectfully traverse the rejection.

The specification of Na 2 is essentially the same as that of Na 1. Similarly, Na 2's composition comprises a cloud point modifier to "increase the cloud point of the surface modifier" to prevent agglomeration of the nanoparticulate drug particles. *See*, for example, page 2, lines 29-33. Therefore, Na 2 does not teach the claimed composition comprising an osmotically active crystal

growth inhibitor to prevent crystal growth of the nanoparticualte drug particles ***at ambient temperatures***. Accordingly, the rejection under § 102(b) should be withdrawn.

V. Rejection of Claims under 35 U.S.C. §103(a)

Claims 1-45 are rejected under 35 U.S.C. 103(a) for allegedly being obvious over Na 1 and Na 2 in view of U.S. Patent Publication No. 2005/0004049 by Liversidge *et al.* Applicants respectfully traverse the rejection.

As discussed in the foregoing paragraphs, neither Na 1 nor Na 2 teaches a composition comprising an osmotically active crystal growth inhibitor to prevent crystal growth of the nanoparticulate drug particles ***at ambient temperatures***. The secondary Liversidge reference does not compensate for the stated deficiency of the primary references, therefore, the cited art does not render the claimed invention obvious. Applicants respectfully request withdrawal of the rejection.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith,

Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date July 9, 2007

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